

ATTACHMENT D

Marked Up Replacement Claims

Following herewith is a marked up copy of each rewritten claim.

13. (Amended) A method for determining the susceptibility of a NIDDM patient toward sulfonylurea therapy comprising :

a) obtaining a sample from a NIDDM patient, said sample comprising nucleic acid molecules containing the fragment of the *SUR1* gene comprising the nucleotide in position -3 of ~~intron~~ exon 16,

b) detecting the presence or the absence of the ~~-3e -3t~~ allele of ~~intron~~ exon 16,

whereby the presence of at least one ~~-3e -3t~~ allele identifies a NIDDM patient with a higher susceptibility toward sulfonylurea therapy.

14. (Amended) The method according to claim 13, further comprising prior to step b) the step of amplifying said nucleic acid molecules using amplification primers that selectively anneal to and amplify a portion of said gene comprising the nucleotide in position -3 of ~~intron~~ exon 16.

15. (Amended) The method according to claim 13, further comprising prior to step b) the step of amplifying said nucleic acid molecules using as amplification primers, the nucleic acid fragments of sequence SEQ ID N° 2 and SEQ ID n° 3, that selectively anneal to and amplify a portion of said gene comprising the nucleotide in position -3 of ~~intron~~ exon 16.

16. (Amended) The method of claim 13, wherein said detecting step b) comprises sequencing all or part of the sequence of ~~intron-46~~ 15 comprising said -3 nucleotide.

17. (Amended) The method of claim 13, wherein said detecting step b) comprises contacting the nucleic acid molecules with a nucleic acid probe that selectively

hybridizes to a portion of ~~said 16~~ intron 15 of *SUR1* gene containing nucleotide -3 as shown in sequence SEQ ID n° 1 under hybridization conditions.

18. (Amended) The method of claim 13, wherein the detecting step b) comprises performing a restriction endonuclease digestion of said nucleic acid molecules thereby yielding a nucleic acid digest and contacting the digest with a nucleic acid probe that selectively hybridizes to a portion of ~~said~~ intron 15 of said *SUR 1* gene combining nucleotide -3 as showed in sequence SEQ ID n° 1.

19. (Amended) The method of claim 13, wherein said detecting step b) comprises obtaining a first gene fragment comprising nucleotide -3 of ~~intron~~ exon 16 isolated from said human sample and a second gene fragment comprising nucleotide ~~-3t~~ -3c of ~~intron~~ exon 16, said second fragment corresponding to said first fragment, forming single-stranded DNA from said *SUR1* gene fragment and from said second *SUR1* gene fragment, electrophoresing said single-stranded DNAs on a denaturing polyacrylamide gel, comparing the mobility of said single-stranded DNAs on said gel to determine if said single-stranded DNA from said first *SUR1* gene fragment is shifted relative to said second *SUR1* gene fragment, and optionally sequencing said single-stranded DNA from said first *SUR1* gene fragment having a shift in mobility.

20. (Amended) The method of claim 13 wherein said detecting step b) comprises obtaining a first gene fragment comprising nucleotide -3 of ~~intron~~ exon 16, isolated from said human sample and a second fragment comprising nucleotide ~~-3c~~ -3t of ~~intron~~ exon 16, said second fragment corresponding to said first fragment, forming single-stranded DNA from said *SUR1* gene fragment and from said second *SUR1* gene fragment, electrophoresing said single-stranded DNAs on a denaturing polyacrylamide gel, comparing the mobility of said single-stranded DNAs on said gel to determine if said single-stranded DNA from said first *SUR1* gene fragment has the same mobility as the said second *SUR1* gene fragment, and optionally sequencing said single-stranded DNA from said first *SUR1* gene fragment.

21. (Amended) The method of claim 13 wherein said detecting step b) comprises amplifying all or part of a *SUR1* gene in said sample using a primer specific for allele—3e-3t and detecting the presence of an amplified product, whereby the presence of said product indicates the presence of said allele in the sample.

22. (Amended) A kit for determining the susceptibility of a NIDDM patient toward sulfonylurea therapy comprising a pair of oligonucleotide primers specific for amplifying all or part of the *SUR1* gene comprising nucleotide -3 of ~~intron~~ exon 16, and instructions relating to detecting the presence of a—3e-3t allele of ~~intron~~ exon 16 and correlating the presence of a—3e-3t allele with a higher susceptibility toward sulfonylurea therapy.

23. (Amended) The kit according to claim 22 comprising a restriction enzyme that specifically cuts fragments comprising nucleotide -3c/nucleotide -3t, and reagents able to detect the presence of a cleaved fragment, the presence of a cleaved fragment being indicative of a higher susceptibility toward sulfonylurea therapy—(3e)/a (-3t)/a lower susceptibility toward sulfonylurea therapy—(3t) (-3c).

24. (Amended) The kit according to claim 22 comprising *Pst* I as restriction enzyme that specifically cuts fragments comprising nucleotide -3c/nucleotide -3t, and reagents able to detect the presence of a cleaved fragment, the presence of a cleaved fragment being indicative of a higher susceptibility toward sulfonylurea therapy—(3e)/a (-3t)/a lower susceptibility toward sulfonylurea therapy—(3t) (-3c).